REMARKS

In the Office Action of June 25, 2008, the Examiner rejected claims 6-28 under35 U.S.C. § 112, first paragraph, for lack of enablement. As the Examiner acknowledges, the present invention is directed to a method of administering a live attenuated bacterial vaccine to a mammal by injecting the vaccine into a submucosal layer of the mammal. The Examiner further acknowledges that the invention encompasses a method for reducing the amount of adverse reaction in a mammal at the injection site of a live attenuated bacterial vaccine by administering the vaccine submucosally. The Examiner objects that the claimed invention encompasses the use of any and all attenuated bacterial vaccines although the specification only discloses the use of *Streptococcus equi* attenuanted strains TW928 and TW928/sls.

The rejection for lack of enablement is respectfully traversed. It may be noted that in the examples provided, in addition to illustrating the advantage of using two strains of *Streptococcus equi*, Examples 2 and 3 disclose the use of *Streptococcus zooepidemicus* and *Actinomyces pyogenes*. Moreover, the objective of the present invention is the reduction of adverse reactions at the injection site of a live attenuated bacterial vaccine, not the preparation of vaccines.

Applicants respectfully submit that the ordinary practitioner knows well that he can select from any number of available live attenuated bacterial vaccines. That is well within the skill of the art and it is not required for Applicants to teach the preparation of live attenuated bacterial vaccines as they are readily available. What was not known, and this is taught by Applicants, is a method for avoiding adverse reactions at the injection site of live vaccines, which result in unsightly lesions and, in the case of food animals, create a recognized significant problem in lost meat value. It had not previously been recognized that such adverse reactions could be reduced, short lived, or avoided by administering the vaccine submucosally rather than subcutaneously or intramuscularly.

Although it may be correct that the efficacy of an attenuated bacterial vaccine cannot be absolutely predicted, as noted above, attenuated bacterial vaccines are not the invention presently

claimed. It is the use of known vaccines in methods by which expected adverse reactions are now avoided. Accordingly, it is respectively submitted that the method as claimed is fully enabled by the disclosure and it is requested that the rejection under 35 U.S.C. 112, second paragraph, be withdrawn.

Claims 6, 9 and 21 stand rejected under 35 U.S.C. § 102(b) for anticipation by Walker. Walker is relied on for teaching submucosal injection of S.mutans in monkeys.

The rejection over Walker is respectfully traversed. For purposes of anticipation a reference must teach all elements of the claimed invention. Walker teaches the administration of **killed** (formalized) *S.mutans*. The present invention is directed to reducing adverse reactions caused by the administration of **live attenuated bacterial vaccines**.

Beyond not teaching the method presently claimed, the adverse reactions that are avoided by the method of the present invention would not characterize the activities described by Walker. The adverse reactions to which the present invention is addressed are characteristic of the administration of live bacterial vaccines that replicate at the injection site and, therefore, cause abscess formation when administered intramuscularly. Applicants discovered that adverse reactions can be avoided by administering the same vaccine submuscosally. Walker, by contrast, administered killed vaccines. Adverse reactions associated with live vaccines would not be present with killed vaccines whether administered subcutaneously, which Walker also taught, or intramuscularly, which was not disclosed in that reference, or, of course, submucosally. As Walker administered a killed vaccine he could not have discovered or disclosed Applicants' invention.

Claim 7-8, 11-20 and 23-28 stand rejected under 35 U.S.C. 103(a) for being obvious over Walker when taken further in view of Stocker and Hartford. In addition to Walker's disclosure of administering a [killed] bacterial vaccine submucosally, Stocker is relied on for teaching live attenuated bacterial vaccines for Salmonella used in a wide variety of animals. Hartford is relied on for teaching a method for protecting horses against *Streptococcus equi* by oral administration of a live *Streptococcus equi* TW928 strain. The Examiner concluded that it would be obvious to one of ordinary skill in the art to modify the invention of Walker with Stocker or Hartford by

substituting the killed *S.mutans* vaccines with attenuated live bacterial vaccines in a variety of domestic animals and saw motivation in the desire to generate an immune response against bacteria of interest in domestic animals, and further being motivated to inject attenuated bacterial vaccines to bypass the mucosal barrier, concluding that one would have a reasonable expectation of success since the use of oral vaccines had been routine in the art of the time the invention was made and the invention, therefore, was *prima facie* obvious in view of the art of record.

The invention is not in any way *prima facie* obvious in view of the cited art. Walker teaches the administration of a killed vaccine. With a killed vaccine there would be no replication of bacteria and, therefore, no reason to try to solve the problem of adverse reactions at the injection site. Stocker teaches live attenuated bacterial vaccines but does not teach administration submucosally. Similarly, Hartford may teach a vaccine comprising one of the *Streptococcus equi* strains used in Applicants' examples, but again there is no teaching of administering this vaccine submucosally. In fact, it is recommended that it be administered in the nose by spraying, although administration intramuscularly, subcutaneously or intradermally are also mentioned as possibilities (page two, lines 11-17).

None of the cited references teaches a concern for injection cite lesions. There is no apparent motivation for seeking a way to avoid them when using live attenuated bacterial vaccines. There is no suggestion that lesions can be avoided by submucosal administration. There is nothing in the combination of references to motivate the ordinary practitioner to administer live vaccines, such as the live attenuated bacterial vaccines of Stocker or Hartford, submucosally.

Walker would lead one to consider submucosal administration for killed vaccines. However, the skilled practitioner, being aware that live attenuated vaccines result in the replication of bacteria at the site of injection, causing injection site lesions, and being aware that killed vaccines do not result in replication or significant adverse reactions, would find nothing in Walker to suggest that adverse reactions at the injection site could be avoided by selecting submucosal administration in place of intradermal, intramuscular or subcutaneous administration.

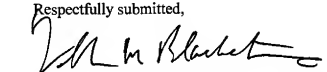
In view of the above, with the present amendments, it is submitted that claims 9-11, 13-16

and 20-28 are in condition for allowance. Favorable action is solicited.

Should it be believed that a conference would be helpful in advancing the prosecution of this application, the Examiner is invited to telephone Applicants' attorney at the number below.

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Respectfully submitted,



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